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AEDER, SEAN E	

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1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,350	KRASNOPEROV ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-29,32-34,38-56 and 63-68* is/are pending in the application.

4a) Of the above claim(s) *38-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29,32-34 and 63-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Remarks filed 1/7/09 in response to the Office Action of 10/7/08 are acknowledged and have been entered.

Claims 26-29, 32-34, 38-56, and 63-68 are pending.

Claims 38-56 have been withdrawn.

Claims 26-29, 32-34, and 63-68 are currently under examination.

Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26-29, 32-34, 63, and 65-68 remain rejected under 35 U.S.C. 103(a), as being unpatentable over Stephenson et al (BMC Molecular Biology, 12/21/01, 2(15): 1-9) in view of Flanagan et al (WO 96/26958; 9/6/96) and Genentech (WO 00/30673; 6/2/00), for the reasons stated in the Office Action of 10/7/08 and for the reasons set-forth below.

Claim 26 is drawn to a monoclonal antibody which binds to an extracellular domain of an EphB4 protein and promotes apoptosis in a tumor cell, wherein the antibody is selected from bispecific, single-chain, chimeric, human, syngeneic, and humanized antibodies. Claim 27 is drawn to the antibody of claim 26, wherein the

antibody inhibits the interaction between Ephrin B2 and EphB4. Claim 28 is drawn to the antibody of claim 26 wherein the antibody inhibits clustering of EphB4. Claim 29 is drawn to the antibody of claim 26, wherein the antibody inhibits phosphorylation of EphB4. Claim 32 is drawn to a pharmaceutical composition comprising the antibody of claim 26, and a pharmaceutically acceptable carrier. Claim 33 is drawn to a cosmetic composition comprising the antibody of claim 26 and a pharmaceutically acceptable carrier. Claim 34 is drawn to a diagnostic kit comprising the antibody of claim 26 and a carrier. Claim 63 is drawn to a cell expressing the antibody of claim 26. Claim 65 is drawn to the antibody of claim 26 further comprising a label attached thereto. Claim 66 is drawn to the antibody of claim 65 wherein the label is selected from a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Claim 67 is drawn to the antibody of claim 26, wherein the antibody inhibits angiogenesis. Claim 68 is drawn to the antibody of claim 26 wherein the antibody promotes tumor regression.

Stephenson et al teaches a polyclonal antibody and antibody kit available from Santa Cruz Biotechnology Inc (page 8 left column), EphB4 (H-200). As evidenced by Santa Cruz Biotechnology Inc datasheet for EphB4 (H-200), EphB4 (H-200) was raised against amino acids 201-400 mapping within the extracellular domain of human EphB4. Further, the datasheet states that the antibody is provided in a kit comprising a composition comprising the pharmaceutically acceptable carrier PBS. Further, Stephenson et al teaches that EphB4 protein is expressed on colon cancer tissues and either not at all, or in only low levels, in normal tissue (see Figure 4, in particular). Stephenson further teaches that therapies targeting EphB4 protein could be used in

anticancer treatments (see page 2 left column, in particular). Due to the expression pattern of EphB4 protein, one of skill in the art would recognize that antibodies against EphB4 protein would also be used in methods of diagnosing colon cancer.

Stephenson does not specifically teach: monoclonal antibodies that specifically bind to an extracellular domain of EphB4 that promote apoptosis in a tumor cell that are selected from bispecific, single-chain, chimeric, human, syngeneic, and humanized antibodies; wherein the antibody inhibits the interaction between Ephrin B2 and EphB4; wherein the antibody inhibits clustering of EphB4; wherein the antibody inhibits phosphorylation of EphB4; said antibodies in a composition comprising a pharmaceutical carrier; cells expressing said antibodies; said antibodies further comprising a label such as a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor; wherein said antibodies inhibit angiogenesis; or wherein the antibodies promote tumor regression. However, these deficiencies are made up in the teachings of Flanagan et al and Genentech et al.

Flanagan et al members of the Eph receptor family play a role in growth regulation, differentiation, and oncogenesis (lines 19-23 on page 2, in particular). Flanagan et al further teaches labeled antibodies wherein the label is an enzyme, a radioactive substance, a chromophore, or a fluorochrome (lines 1-5 on page 20, in particular). Flanagan et al further teaches therapeutic antibodies that inhibit binding of ligands to Eph receptors (lines 7-19 on page 20, in particular).

Genentech teaches inhibiting angiogenesis and treating cancer in a mammal by administering an Eph receptor antagonist (pages 2-3, in particular). Genentech further

identifies EphB4 as an Eph receptor and Ephrin B2 as a ligand for EphB4 (lines 30-32 on page 2, in particular). Genentech further teaches said antagonist as an antibody (page 6, in particular). Genentech further teaches said antagonist antagonizes the interaction between an Eph receptor and an Eph ligand, prevents or reduces tyrosine phosphorylation of Eph receptor, prevents or reduces angiogenesis, and eradicates or reduces tumor size (page 11, in particular). Genentech further teaches antibodies as monoclonal and bispecific, chimeric, and humanized (lines 26-29 on page 7 and lines 6-27 on page 8, in particular). Genentech further teaches cells expressing said antibodies and animals expressing said antibodies (line 2 on page 8, in particular). Genentech further teaches said antibodies in pharmaceutically acceptable carriers (lines 36-40 on page 22, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the teachings of Stephenson et al with those of Flanagan et al and Genentech to produce monoclonal and bispecific, chimeric, and humanized antibodies that specifically bind the extracellular domain of EphrinB4 and are labeled with a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor, wherein said antibodies antagonize the interaction between EphrinB4 and Ephrin B2, prevent and reduce tyrosine phosphorylation of EphrinB4, prevent and reduce angiogenesis, and eradicate and reduce tumor size in order to diagnose and treat colon cancer because Stephenson et al teaches that targeting EphB4 protein is a means of treating cancer, antibodies against EphB4 protein would be used to diagnose colon cancer in view of the teachings of Stephenson et al, and EphB4 antagonist antibodies

identified by an ability to bind the extracellular domain of EphrinB4 and that are labeled with a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor, wherein said antibodies antagonize the interaction between EphrinB4 and Ephrin B2, prevent and reduce tyrosine phosphorylation of EphrinB4, prevent and reduce angiogenesis, and eradicate and reduce tumor size would be therapeutically and diagnostically beneficial to humans with colon cancer. Further, one would be motivated to produce cells expressing said antibodies, by means taught by Genentech et al, in order to generate said antibodies. Further, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings of Stephenson et al with those of Flanagan et al and Genentech to produce compositions comprising a pharmaceutical carrier and monoclonal and bispecific, chimeric, and humanized antibodies that specifically bind the extracellular domain of EphrinB4 and are labeled with a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor, wherein said antibodies antagonize the interaction between EphrinB4 and Ephrin B2, prevent and reduce tyrosine phosphorylation of EphrinB4, prevent and reduce angiogenesis, and eradicate and reduce tumor size in order to diagnose and treat colon cancer because Stephenson teaches that targeting EphB4 protein is a means of treating cancer, antibodies against EphB4 protein would diagnose colon cancer and EphB4 antagonist antibodies identified by an ability to bind the extracellular domain of EphrinB4 and that are labeled with a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor, wherein said antibodies antagonize the interaction between EphrinB4 and Ephrin B2, prevent and reduce

tyrosine phosphorylation of EphrinB4, prevent and reduce angiogenesis, and eradicate and reduce tumor size would be therapeutically and diagnostically beneficial to humans with colon cancer. Further, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings of Stephenson et al with those of Flanagan et al and Genentech to produce cells expressing said antibodies, in order to generate said antibodies because Genentech teaches the means required to produce said antibodies. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Further, one of skill in the art would recognize that the antibodies taught by the combined teachings above would inhibit clustering of EphB4 and promote apoptosis, as such effects would be found in the antibodies taught by the combined teachings that would sterically hinder clustering and eradicate and reduce tumor size by apoptosis. Further, *as evidenced by* Xi et al (Clinical Cancer Research, June 2005, 11(12):4305-4315), EphB4 normally phosphorylates proteins such as Akt that are known to promote tumor cell survival (page 4314, in particular). Therefore, disruption of EphB4 phosphorylation by the antibodies produced by the combined teachings above would lead to a reduction in tumor cell survival and a shift towards apoptosis, a result obtained when siRNA reduces the expression of EphB4 in cultured cells (Figure 4, in particular). Absent a showing otherwise, the antibodies taught by the combined teachings above would inhibit clustering of EphB4 and promote apoptosis. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that

the antibodies of the prior art do not possess the same characteristics as the claimed antibodies. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed antibodies are different from those taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989).

In the Reply of 1/7/09, Applicant correctly points-out that Stephenson et al does not teach a monoclonal antibody which promotes apoptosis in a tumor cell. Applicant further correctly points-out that the cited section of Flanagan teaches antibodies against the EIF-2 ligand and not antibodies against the EphB4 receptor. Applicant further correctly points-out that Genentech does not teach an isolated monoclonal antibody which binds to an extracellular domain of an EphB4 protein or an anti-EphB4 antibody which promotes apoptosis in tumor cells. Further, Applicant argues that the combination of Stephenson et al, Flanagan et al, and Genentech fails to teach all elements of independent claim 26, such as a monoclonal antibody against EphB4 that promotes apoptosis in tumor cells. Applicant further argues that the Examiner has not provided any factual basis and/or technical reasoning to reasonably support the assertion that the antibodies taught by the combination of Stephenson et al, Flanagan et al, and Genentech are capable of promoting apoptosis in tumor cells. Applicant further cites the Board and states that it is well known in the art that antibodies are unpredictable in nature. Applicant further cites the specification at pages 102-104 and Figure 59 and argues that one of skill in the art would know that not all antibodies against EphB4 are capable of promoting apoptosis in a tumor cell. Applicant further

argues that in view of the unpredictable nature of antibodies, the lack of evidence that EphB4 antibodies could promote apoptosis, and the lack of guidance of how to make and select EphB4 antibodies with a particular feature (e.g., apoptosis promoting activity), a skilled artisan could not reasonably expect that apoptosis-promoting EphB4 antibodies would be successfully made. Applicant further argues that there is no suggeston for a skilled artisan to make apoptosis-promoting EphB4 monoclonal antibodies as recited in claim 26.

The arguments found in the Reply of 1/7/09 have been carefully considered, but are not deemed persuasive. In regard to the arguments that the combination of Stephenson et al, Flanagan et al, and Genentech fails to teach a monoclonal antibody against EphB4 that promotes apoptosis in tumor cells and that the Examiner has not provided any factual basis and/or technical reasoning to reasonably support the assertion that the antibodies taught by the combination of Stephenson et al, Flanagan et al, and Genentech are capable of promoting apoptosis in tumor cells, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the teachings of Stephenson et al with those of Flanagan et al and Genentech to produce monoclonal antibodies that specifically bind the extracellular domain of EphrinB4 and that antagonize the interaction between EphrinB4 and Ephrin B2, prevent and reduce tyrosine phosphorylation of EphrinB4, prevent and reduce angiogenesis, and eradicate and reduce tumor size in order to diagnose and treat colon cancer because Stephenson et al teaches that targeting EphB4 protein is a means of treating cancer, antibodies against EphB4 protein would be used to diagnose colon cancer in

view of the teachings of Stephenson et al, Genentech teaches antagonizing the interaction between an Eph receptor and an Eph ligand, prevents or reduces tyrosine phosphorylation of Eph receptor, prevents or reduces angiogenesis, and eradicates or reduces tumor size (page 11, in particular), and EphB4 antagonist antibodies identified by an ability to bind the extracellular domain of EphrinB4 and antagonize the interaction between EphrinB4 and Ephrin B2 which prevent and reduce tyrosine phosphorylation of EphrinB4, prevent and reduce angiogenesis, and eradicate and reduce tumor size would be therapeutically and diagnostically beneficial to humans with colon cancer. Further, one of skill in the art would recognize that the antibodies taught by the combined teachings above would inhibit clustering of EphB4 and promote apoptosis, as such effects would be found in the antibodies taught by the combined teachings that would sterically hinder clustering and antagonize the interaction between an Eph receptor and an Eph ligand, prevent or reduces tyrosine phosphorylation of Eph receptor, prevent or reduces angiogenesis, and eradicate or reduces tumor size. Further, *as evidenced by* Xi et al (Clinical Cancer Research, June 2005, 11(12):4305-4315), EphB4 normally phosphorylates proteins such as Akt that are known to promote tumor cell survival (page 4314, in particular). Therefore, disruption of EphB4 phosphorylation by the antibodies produced by the combined teachings above would lead to a reduction in tumor cell survival and a shift towards apoptosis, a result obtained when siRNA reduces the expression of EphB4 in cultured cells (Figure 4, in particular). Absent a showing otherwise, the antibodies taught by the combined teachings above would inhibit clustering of EphB4 and promote apoptosis. The office does not have the

facilities and resources to provide the factual evidence needed in order to establish that the antibodies of the prior art do not possess the same characteristics as the claimed antibodies. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed antibodies are different from those taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989).

In regards to the argument that it is well known in the art that antibodies are unpredictable in nature, the antibodies generated and selected by the combined teachings of Stephenson et al, Flanagan et al, and Genentech have particular characteristics. Such characteristics include: (1) an ability to bind the extracellular domain of EphrinB4; (2) an ability to antagonize the interaction between EphrinB4 and Ephrin B2; (3) an ability to prevent and reduce tyrosine phosphorylation of EphrinB4; (4) an ability to prevent and reduce angiogenesis; and (5) an ability to eradicate and reduce tumor size. Such selected antibodies would also promote apoptosis because, *as evidenced by* Xi et al, EphB4 normally phosphorylates proteins such as Akt that are known to promote tumor cell survival (page 4314, in particular). Further, disruption of EphB4 phosphorylation by the antibodies produced by the combined teachings above would lead to a reduction in tumor cell survival and a shift towards apoptosis, a result obtained when siRNA reduces the expression of EphB4 in cultured cells (Figure 4, in particular).

In regards to the citation of the specification at pages 102-104 and Figure 59 and the argument that one of skill in the art would know that not all antibodies against

EphB4 are capable of promoting apoptosis in a tumor cell, the Examiner agrees that not all antibodies against EphB4 are capable of promoting apoptosis in a tumor cell. However, antibodies generated and selected by the combined teachings of Stephenson et al, Flanagan et al, and Genentech have particular characteristics. Such characteristics include: (1) an ability to bind the extracellular domain of EphrinB4; (2) an ability to antagonize the interaction between EphrinB4 and Ephrin B2; (3) an ability to prevent and reduce tyrosine phosphorylation of EphrinB4; (4) an ability to prevent and reduce angiogenesis; and (5) an ability to eradicate and reduce tumor size. Such selected antibodies would also promote apoptosis because, *as evidenced by* Xi et al, EphB4 normally phosphorylates proteins such as Akt that are known to promote tumor cell survival (page 4314, in particular). Further, disruption of EphB4 phosphorylation by the antibodies produced by the combined teachings above would lead to a reduction in tumor cell survival and a shift towards apoptosis, a result obtained when siRNA reduces the expression of EphB4 in cultured cells (Figure 4, in particular). Further, it has not been demonstrated that the antibodies disclosed on pages 102-104 and Figure 59 share such characteristics.

In regards to the argument that a skilled artisan could not reasonably expect that apoptosis-promoting EphB4 antibodies would be successfully made because of the unpredictable nature of antibodies, the lack of evidence that EphB4 antibodies could promote apoptosis, and the lack of guidance of how to make and select EphB4 antibodies with a particular feature (e.g., apoptosis promoting activity), apoptosis-promoting EphB4 antibodies would be successfully made by the combined teachings of

Stephenson et al, Flanagan et al, and Genentech because antibodies generated and selected by the combined teachings of Stephenson et al, Flanagan et al, and Genentech have particular characteristics. Such characteristics include: (1) an ability to bind the extracellular domain of EphrinB4; (2) an ability to antagonize the interaction between EphrinB4 and Ephrin B2; (3) an ability to prevent and reduce tyrosine phosphorylation of EphrinB4; (4) an ability to prevent and reduce angiogenesis; and (5) an ability to eradicate and reduce tumor size. Such selected antibodies would also promote apoptosis because, *as evidenced by* Xi et al, EphB4 normally phosphorylates proteins such as Akt that are known to promote tumor cell survival (page 4314, in particular). Further, disruption of EphB4 phosphorylation by the antibodies produced by the combined teachings above would lead to a reduction in tumor cell survival and a shift towards apoptosis, a result obtained when siRNA reduces the expression of EphB4 in cultured cells (Figure 4, in particular).

In regards to the argument that there is no suggesting for a skilled artisan to make apoptosis-promoting EphB4 monoclonal antibodies as recited in claim 26, KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See Ex parte Smith, --USPQ2d--, slip op. at 20 (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf). Reasons to generate and select antibodies that would promote apoptosis of tumor cells are discussed above.

Claims 26-29, 32-34, 63, and 64-68 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Stephenson et al (BMC Molecular Biology, 12/21/01, 2(15): 1-9) in view of Flanagan et al (WO 96/26958; 9/6/96) and Genentech (WO 00/30673; 6/2/00) as applied to claims 26-29, 32-34, 63, and 65-68 above, and further in view of Sola et al (Journal of Virology, May 1998, 3762-3772), for the reasons stated in the Office Action of 10/7/08 and for the reasons set-forth below.

Teaching of Claims 26-29, 32-34, 63, and 64-68 by the combined teachings of Stephenson et al, Flanagan et al, and Genentech is discussed above.

The combined teachings of Stephenson et al, Flanagan et al, and Genentech do not specifically teach a non-human transgenic animal expressing the antibody of claim 26. However, this deficiency is made up in the teachings of Sola et al.

Sola et al teaches producing recombinant monoclonal antibodies in mice (see pages 3767-3768, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to produce non-human transgenic animals that express the antibodies of Stephenson et al, Flanagan et al, and Genentech because said animals would provide a means of producing antibodies with diagnostic and therapeutic benefit. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for producing non-human transgenic animals that express the antibodies of Stephenson et al, Flanagan et al, and Genentech because Sola et al teaches producing recombinant monoclonal antibodies in mice (see pages 3767-3768, in particular). Therefore, the invention as a whole would have been prima

facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

In the Reply of 1/7/09, Applicant argues that Sola et al does not make-up alleged deficiencies of Stephenson et al, Flanagan et al, and Genentech.

The arguments found in the Reply of 1/7/09 have been carefully considered, but are not deemed persuasive. The alleged deficiencies of Stephenson et al, Flanagan et al, and Genentech are addressed above.

Summary

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Primary Examiner, Art Unit 1642